

Appl. No. 09/872,702
Amendment dated July 8, 2003
Reply to Final Office Action of April 11, 2003

REMARKS

Applicants have received and reviewed a Final Office Action dated April 11, 2003. Applicants request entry of this Amendment and Response and reconsideration of the rejection of the claims.

Applicants have cancelled claims 11 and 47 without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in a continuation application.

Applicants have amended claims 1, 10, 12, 13, 22, 30, 31, 35, 46, 48, 49, 50 and 51. Applicants submit the amendments are supported throughout the specification and do not raise any issues of new matter.

Claim Objection

The Examiner objected to claim 31 as being of improper dependent form. Applicants submit that claim 31 is not a dependent claim, but is an independent claim drawn to a host cell. Applicants, therefore, request withdrawal of the objection of this claim.

35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 1-13, 22, 30, 31 and 35-51 under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse the rejection.

The Examiner contends that the uses of the word "in" and "on" in the claims is inconsistent. Applicants do not concede the priority of the rejection, but have amended the claims to use the word "in" consistently.

The Examiner rejected claims 10, 11, 22, 46 and 47. The Examiner contends that 1) the claims do not clearly define an order the two things are done; 2) the claims do not have a step comparing the result between the two populations; and 3) the Examiner contends that it is unclear that there would exist any epitopes that would be present in a naïve animal, but not in an animal dosed with a therapeutic polypeptide. Applicants submit claims 11 and 47 have been cancelled rendering the rejection of these claims moot. Applicants have reserved the right to pursue the

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subject matter of these claims in a continuation application. Applicants traverse the rejection with respect to the rest of the claims.

Applicants submit that the steps of claims 10, 22 and 46 do not require nor do they need to be conducted in any particular order. For example, in some embodiments, the antibody or population of antibodies from a naïve human subject and from a human subject dosed with the therapeutic polypeptide can be obtained from different subjects, and compared simultaneously. Thus, Applicants submit determination of the epitopes in the polypeptide that bind to antibodies from naïve and dosed subjects does not require any order.

With respect to the step of comparing the binding specificities of the two types of antibodies, Applicants have amended the claims. Applicants do not concede the priority of the rejection and have amended the claim solely to expedite prosecution.

With respect to the Examiner's contention that it is not clear that there would exist any epitopes identified in naïve subjects and not in subjects dosed with the polypeptide, Applicants submit that there could be epitopes that differ in these subjects. For example, Applicants have indicated that it was surprising that antibodies to endogenous polypeptides existed in naïve subjects. The processes that lead to the development of such antibodies are not yet well characterized, therefore, it is possible that different epitopes might be recognized in a naïve subject as compared to a subject dosed with the polypeptide.

In addition, in Example 2, Applicants note that several individuals with preformed antibodies did not have antibody related thrombocytopenia (see the specification at page 49, line 11 to line 20). In some cases, antibodies in patients dosed with the thrombopoietin were directed at the N-terminal end of the molecule rather than the C-terminal end. Thus, it is clear that different epitopes can be identified in naïve versus dosed populations.

The Examiner rejected claim 12 and 48 because the Examiner contends it is unclear how an antibody could fail to affect at least one substantial therapeutic activity of the polypeptide. Applicants submit that a therapeutic activity is defined in the application as biological activity of a polypeptide, preferably a biological activity which correlates with a therapeutic activity. (See page 8, lines 8 to 10). Therapeutic activity is defined as having an in vivo effect or function. Applicants submit the claims are directed to biological activities or functions of polypeptides and not to all

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biological properties of the polypeptide. Applicants submit that clearance or half life of a polypeptide is a biological property of the polypeptide, but not a biological activity. Applicants submit one of skill in the art reading the specification would understand the meaning of claim 12 and claim 48.

The Examiner rejected claim 22 as an incomplete method claim. Applicants do not concede the propriety of the rejection, but have amended the claim to address the Examiner's rejection.

The Examiner rejected claim 30 and other claims as incomplete method claims. Applicants do not concede the propriety of the rejection but have amended the claims to address the Examiner's rejection.

Based on the foregoing, Applicants request withdrawal of all of the 35 U.S.C. § 112, second paragraph, rejections of the claims.

Summary

Applicants submit the claims are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicants' representative if prosecution may be assisted.

Respectfully submitted,

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